REMARKS

Applicant is submitting with this Amendment substitute pages for the specification and a marked up version of the claims that includes the changes made in the Preliminary Amendment.

The claims were objected to with respect to the recitation of a normality range. The claims were also rejected under 35 U.S.C. 112, second paragraph, in that the normality range in claims 1 and 11 were not supported by the specification and that claim 9 lacked antecedent basis for "the filtering step." Initially, Applicant disagrees with the rejection of claims 1 and 12 as being unsupported by the specification as the range of salt normality recited in the claims as filed is to be deemed a part of the original disclosure. In any event, claims 1 and 12 have been amended along the lines suggested by the Examiner and to recited a normality range that is supported explicitly in the specification. Claim 9 has been amended to add an antecedent basis for "the filtering step." Reconsideration and withdrawal of the 112 rejection in light of the foregoing amendments and remarks is respectfully requested.

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable of Ryan et al. in view of Lunder. This ground of rejection is traversed.

In a personal interview with Examiner Patten on December 5, 2003, it was agreed that Ryan et al. did not suggest the removal of alcohol from the purification procedure, and therefore the ordinary artisan would not have been motivated to perform the procedure as recited in claim 2 wherein the extraction solution was specified to be alcohol-free. Claims 1 and 12 have been amended to include the recitation that the extraction solution be alcohol-free. In view of this amendment, all claims are believed to be patentably distinct from Ryan et al. and all other cited references. Reconsideration and withdrawal of the 103(a) rejection is respectfully requested.

The application has been amended to correct minor informalities, to further distinguish the application over the prior art, and to more particularly point out and distinctly claim the subject matter which Applicant regards as the invention so as to place the application, as a whole, into a prima facie condition for allowance. Great care has been taken to avoid the introduction of new subject matter into the application as a result of the foregoing modifications.

Accordingly, the purpose of the claimed invention is not taught nor suggested by the cited references, nor is there any suggestion or teaching which would lead one skilled in the relevant art to combine the references in a manner which would meet the purpose of the claimed

invention. Because the cited references, whether considered alone, or in combination with one another, do not teach nor suggest the purpose of the claimed invention, Applicant respectfully submits that the claimed invention, as amended, patentably distinguishes over the prior art, including the art cited merely of record.

Based on the foregoing, Applicant respectfully submits that its claims 1, and 3-14, as amended, are in condition for allowance at this time, patentably distinguishing over the cited prior art. Accordingly, reconsideration of the application and passage to allowance are respectfully solicited.

The Examiner is respectfully urged to call the undersigned attorney at (515) 288-2500 to discus the claims in an effort to reach a mutual agreement with respect to claim limitations in the present application which will be effective to define the patentable subject matter if the present claims are not deemed to be adequate for this purpose.

Respectfully submitted,

Date: December 17, 2003

Kent A. Herink
Registration No. 31,025
DAVIS, BROWN, KOEHN,
SHORS & ROBERTS, P.C.
666 Walnut St., Suite 2500
Des Moines, Iowa 50309
Telephone: (515) 288-2500

ATTORNEYS FOR APPLICANT

The second full paragraph on page 3:

Comminution is accomplished by grinding. A target particle size is in the range of 100 to 1500 μm. In this range, product yields were increased and flow characteristics of the slurry were acceptable. Decreasing the particle size below 100 μm resulted in a lower recovery of PI2 and did not improve the flow characteristics. Grinding for an extended period of time also resulted in a reduced PI2 yield, most likely due to an increase in temperature and the release of undesired proteases that reduce the PI2 yield. The formic acid and sodium chloride are efficiently removed during the filtration stage.

The paragraph bridging pages 4 and 5:

The amount of PI2, Kunitz and carboxypeptidase inhibitors was measured using reverse phase HPLC. A Microsorb C-18 column (4.6 mm x 250 mm, 5 μm particles with 300 Angstrom pore size; Varian Analytical Instruments) was used. Two mobile phase solvents were prepared, solvent A was 800 g deionized H_2O, 150 g acetonitrile, and 0.95 grams trifluoroacetic acid, and solvent B was 850 g acetonitrile and 0.85 g trifluoroacetic acid. Approximately 50 mg of the sample was added to 100 ml of solvent A. The sample was vortexed for 30 seconds, and then centrifuged at 10,000 rpm for 10 minutes. The supernatant was collected for RP-HPLC analysis. One hundred μl of the sample was injected into the column, with the pump set at 800 - 2500 psig, and a temperature of 30.0° C. The other flow rate, time, and solvent compositions are as set out in Table 1. The diode array of the detector was set at 220 nm.

The paragraph bridging pages 5 and 6:

Five hundred grams of potato tubers were extracted with 213 ml of 1% formic acid solution in a Waring blender for 2.5 minutes. The slurry was centrifuged at 10,000 rpm for 40 minutes. The liquid was decanted and filtered through #4 Whatman filter paper, yielding 486 g of clarified extract. Fifty grams of this clarified extract was poured into each of six 125 ml Erlenmeyer flasks equipped with magnetic stir bars. The amount of NaCl corresponding to Table 2 was added to each flack and stirred until the salt was dissolved. The flasks were then heated on high with stirring on a hot plate until the temperature of the extract reached 70° C. After ambient cooling to room temperature, the solutions were centrifuged at 12,000 rpm for 5 minutes and then analyzed using the above-described reverse phase HPLC method. The reported level of PI2 was calculated by integrating the area of the PI2 peak. The injection volume was 100 μl and the following equation was used to equate peak areas to protein levels:

$$\text{Protein (mg/ml)} = \left[\left(\frac{\text{peak area}}{4}\right) \times 8.17 \times 10^{-5}\right] + 0.0338$$

The paragraph bridging pages 15 and 16:

A further study examined the yield of PI2 using a variety of grind profiles. The grind profiles examined varied from 300 μm average particle size to 1200 μm average particle size.

Table 14 - Optimization of Grinding Profile and PI2 Yield

Average grind profile	Gap	PI2 yield	Kunitz content	PI2/'Kunitz' purity	Temperature increase
Approx. 300 micron	214 μ	98.55%	105.77%	48.23%	13.1° C
Approx. 500 micron	388 μ	100.00%	100.00%	50.00%	10.4° C
Approx. 700 micron	633 μ	93.68%	97.94%	48.89%	8.8° C
Approx. 900 micron	968 μ	91.32%	94.88%	49.05%	6.7° C
Approx. 1200 micron	1519 μ	86.57%	84.97%	50.47%	5.2° C

Table 14 presents the optimization study for final grind profile with respect to PI2 yield. The yields and purities are normalized to the highest PI2 yield in the sample set. The highest yield was observed at approximately 500 μm average particle size. The PI2/Kunitz purity is also acceptable, only one other grind profile exhibited a higher purity, however with an unacceptable sacrifice in PI2 yield. In order to produce the desired grind profile at the pilot scale, a "Microcut Head Assembly" was used. The final grind profile is determined by several mechanical characteristics of the grinding head, such as the number, spacing and angle of blades in the head as well as the speed and type of impeller. The Microcut head features 190 tungsten carbide blades, each .084 inches thick. This thickness allows for a spacing of .0153 inches (388.62 μ) between each blade. The product is pushed through the spaces between the blades by the impeller. The impeller being used is a "veri-cut" due to its durability and the uniform particle size it produces. This impeller, in conjunction with this head assembly, produces a depth of cut of .0016 inches (40.64 μ). The interaction of the impeller, grinding blades and raw materials generates the friction responsible for the observed temperature rise. A rise of ten degrees was not considered harmful, due to the heat stability of PI2 (70° C for ~~ore~~ more than 3 hours). The depth of cut may vary slightly with the speed of the impeller, which is determined by the motor. For these studies, a consistent grind profile was used to provide an average particle size of approximately 500 μm.